The pigmentation developed in a case of lupus erythematosus which had been under treatment with gold sodium thiosulphate by Doctor Alderson I have observed in other patients, and I am of the opinion that the increase of pigment in this instance is in some way connected with the action of the drug on such a patient. It must be remembered that lupus erythematosus is a highly photosensitive disease of the skin. I also believe that certain types of vitiligo and lupus erythematosus are somewhat related.

The point which I have stressed is that vitiligo may recur after apparent cure, and in two patients whose pictures I have shown you I was able to improve them again by readministration of gold and sodium thiosulphate. A definite amelioration of the vitiligo took place within one week in one patient's appearance after a single dose of the gold. This patient had two subsequent attacks of the vitiligo spaced about a year apart, and response to the treatment of each recurrence was just as spectacular as when the gold sodium thiosulphate was used for the first time.

Investigation of the biochemical reactions of gold and sodium thiosulphate in tissue is being studied at the present time by a reputed expert in this phase of chemistry, with special reference to its action in photosensitive cases, but at the time this article is written the work is but partially finished.

THE LURE OF MEDICAL HISTORY *

ESSAYS ON THE HISTORY OF EMBRYOLOGY†

THE RISE OF EXPERIMENTAL EMBRYOLOGY

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VIII

LEEUWENHOEK

ALTHOUGH Leeuwenhoek wrote in 1682 to the Royal Society, saying "I find in the seed of man, as also of a dog, two different sorts of animalcules, answering the different sexes of male and female," it would be wrong to conclude that this statement was based on a random guess. It is true that he reiterated it and was firm in his belief in animalculism, but his espousal of the latter was based upon many observations and experiments. Leeuwenhoek had no difficulty in finding multitudes of spermatozoa in the vaginae, uteri, and the tubes of various animals at different intervals after coitus, but he failed to find anything answering to an ovum. He examined the reproductive organs of mammalian females of various species both before and after coitus, and examined and injected the uterine tubes in order to learn something about the size of their lumina. He rightly concluded that any object so large as a Graafian follicle could not possibly pass through the tubes and enter the uterus. He also stated that the so-called ova of de Graaf could not be isolated at any time in their development and declared in this connection: "I know some men will even swear that they have found the aforesaid eggs in the tuba fallopiana of beasts. But I need not believe that these round bodies they have seen in it should be drawn from the imagined egg-branch, through the long and very narrow passage of the tuba fallopiana, because some of the bodies are as large as a pea, nay as the whole egg-branch, and of a very firm and compacted substance: but the way through which they should pass is no wider than the compass of a small pin. Again if it were so as is said, these bodies would be found, not by chance, but always when searched for immediately after copulation; but that is so far from being true that it is hardly to be imagined, if we consider how little time is taken up in the copulation of several animals, as a cow, rabbit, etc. In which so short time, nevertheless, ought to be drawn down through a long and narrow passage, a great number of bodies; in some cases two or three, in others six or eight, and more, according to the number of fetuses to be produced."

Leeuwenhoek made a careful attempt to discover an ovum in the Graafian follicles and says that he even showed the "matter contained in the water bladders, which was nothing but transparent moisture mixed with some red blood globules," to a man who had been a companion of de Graaf, to demonstrate to him that the Graafian follicles were not ova as de Graaf claimed. Leeuwenhoek probably was unfortunate in opening immature follicles but he also opened some that were nearly mature, for he says that they looked red. In regard to these he says that when he examined them with a microscope he "saw they were water bladders, one redder than another, and containing some bloody matter, which consisted of glandulous parts, joined together with membranes, having many globules of blood spread among them, by which one of them was become blood red." From this it is evident that Leeuwenhoek, like many of his successors, including Haighton who also was unsuccessful in his search for ova a century later, were decidedly unlucky, for the ova of the mammals which they studied lie within the range of visibility. Since these men were used to "bend their sight," one can only surmise that they failed to recognize the mammalian ovum because it frequently is surrounded by granulosa cells when it is discharged from the ovary. The earlier investigators may also have looked for a larger body although Haighton (1797) knew the size of the blastocyst in the tube and realized that it grew larger as it descended to the uterus. Since the eggs of birds and reptiles are relatively large and also increase in size with the size of the animal, the absence, in mammals, of anything resembling them or the eggs of fish and amphibia, must have been very puzzling. Moreover, the idea that the early mammalian ovum probably was transparent was widespread and also quite generally accepted. Hence a more or less opaque body such as the ovum in the Graafian follicle of some of the domestic mammals such as the dog, for ex-

* A Twenty-five Years Ago column, made up of excerpts from the official journal of the California Medical Association of twenty-five years ago, is printed in each issue of California and Western Medicine. The column is one of the regular features of the Miscellany Department of California and Western Medicine, and its page number will be found on the front cover index.

† This is the eighth paper of a series of essays on this subject. Previous papers were printed in this journal as follows: Part I, in December California and Western Medicine, page 447; Part II, in January number, page 40; Part III, in February number, page 105; Part IV, in March number, page 176; Part V, in April number, page 241; Part VI, in May number, page 341; Part VII, in June number, page 394.

ample, would not be likely to be recognized as such. The idea of the transparency of mammalian ova was derived partly from the conception that the individual organism did not arise from a preformed organized body and from the observation that the tubal ova found, which in fact were blastocysts, were transparent.

Leeuwenhoek also did many experiments to determine the duration of motility of spermatozoa in a number of species and rightly insisted that although Harvey held that the uterus contains nothing after coitus, his experiments abundantly proved that this was incorrect. It is of special interest that Leeuwenhoek found spermatozoa in the cornua of the uterus of a rabbit fifteen minutes after coitus and, since he did not find them through the entire cornua, he rightly surmised that the "seed had not been long enough in the womb and that the animals had not time to disperse themselves through all of it."

From his experiments on the persistence of motility in spermatozoa, Leeuwenhoek inferred that their development into organisms might occur as late as nine or ten days post congressum, provided a spermatozoön found the proper "punctum" in the uterus for its nourishment. He rightly surmised that the uterus may not be in a suitable condition for the reception of spermatozoa at all times.

Although De Graaf thought that the masculine semen was a bearer of volatile salts which brought to the female a vital contact, and although "seventy other persons asserted the same thing," Leeuwenhoek was convinced from his experiments with mating rabbits that they all were mistaken. From these experiments he learned that, contrary to Harvey, de Graaf, and others, spermatozoa were found in the uterus after mating in dogs and rabbits. He found them in the uterus of a rabbit fifteen minutes after coitus and rightly concluded that he could not find them throughout its entire extent because not sufficient time had elapsed. In his search for the ovum, he carefully examined the ovarian vesicles in the rabbit but never found anything but a transparent fluid mixed with blood. He mated rabbits and killed them from six hours to six days after coitus and examined the uteri and tubes for ova without success. However, from his account it is quite clear that he opened implanted blastocysts of a rabbit which had been mated six days previously, without recognizing what he had actually found. Leeuwenhoek probably also found a blastocyst in a sheep, but unfortunately imagined that it contained a lamb in miniature.

Since he could not find ova in the ovaries or tubes or uterus, he concluded that the ovaries existed only for the unburdening of the adjacent organs, saying that if they really were true ovaria, the eggs should be small at first when development began and then gradually increase in size toward the time when the animals begin to procreate.

Leeuwenhoek's experiments with the seeds of plants caused him to declare: "If these distinc-

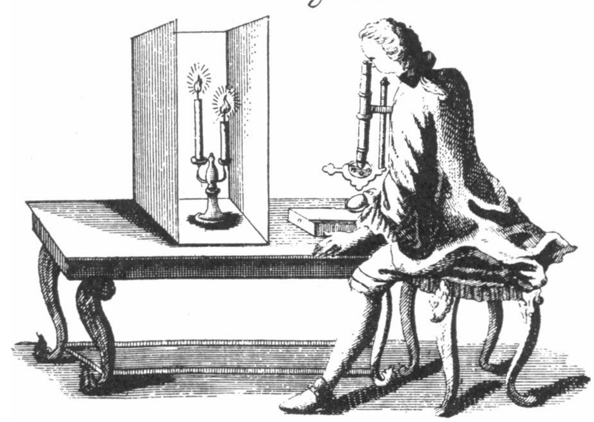

Fig. 3.—Buffon "using his microscope." Ledermuller expressed surprise that he had himself represented in a book, using so poor an instrument.

tions of parts are so soon visible in these small seeds, why should we doubt that production of an animal from the so often named animalcules . . . and, indeed the very minuteness by which one creature is transmitted to another, is incomprehensible?" However, in 1683 he had written: "Other fetuses have a different way of growth; . . . The human fetus, though no larger than a green pea, yet is furnished with all its parts. I have often endeavored to discover the animal coming out of the male seed in the egg of a hen, but have been unsuccessful though some of the globules of the egg were magnified to the size of common apples. This disappointment has put me on the eggs of insects, as the flea and louse, which being very small, may be so much the fitter for this discovery." Leeuwenhoek did not think that the adult form was contained in miniature in the sperm, for he said in 1699, in comment on the statement of a writer in the *Republic of Letters* who claimed as much: "I have a hundred times contemplated the male seed of man; but have not yet discovered any such creature as that aforementioned."

RÉAUMUR'S PLACE IN EXPERIMENTAL EMBRYOLOGY

Réaumur, I think, fills a more important place in experimental embryology than is realized for the literature contains many references to his work. It seems that he placed hen eggs in water at the temperature of incubation in order to learn whether they would hatch under these conditions and found that they would not do so. These experiments were repeated in 1879 by Dareste, who found that development may in fact begin under these conditions but that the embryo is found dead and decomposed after thirty hours of incubation. In one case in which decomposition had not set in, Dareste said he found that development had proceeded abnormally and he called this chick an "omphalocephalic" monster.

Réaumur also attempted to hatch chicks out of unfertilized or wind eggs, and such as possess no hard shell or only an imperfect one, but he failed in this. It seems that he hoped to make use of the heat generated in manure heaps, that lost in bake ovens and in industries, for the commercial hatching of eggs in France. The fact that he designed a thermometer a little less than two decades after Fahrenheit's invention, may also have stimulated his interest in these matters. Réaumur further found that excessive moisture is detrimental to incubation because, as he said, it stopped the pores in the egg shell, but he noticed that after eggs had been incubated under a hen, for ten to fifteen days, incubation could be continued in an excessively moist atmosphere without disadvantage. Whenever he removed some of the shell on the blunt end of the egg at about the seventeenth day of incubation he found that most of the chicks survived in spite of the presence of excessive moisture, and he noticed that thick-shelled eggs like those of ducks suffered most while the more porous and thin-shelled eggs of the turkey suffered least. Eggs with imperfect shells did not hatch at all and he thought that this was because of an excessive loss of moisture.

Réaumur further noticed that molds penetrated the egg shell and that the presence of a putrefying egg in the nest would cause the other eggs to putrefy. By incubating eggs in manure heaps he established that it was not the stench that had the ill effect. He further found that too high and too low temperatures produced more disastrous effects late in the incubation period and that raising the temperature is more detrimental than lowering it. He reported that the smallest eggs never hatched and that the best results were obtained with the fresher and larger ones. He also kept eggs on either end during incubation and stated that no abnormalities could be produced in this way.

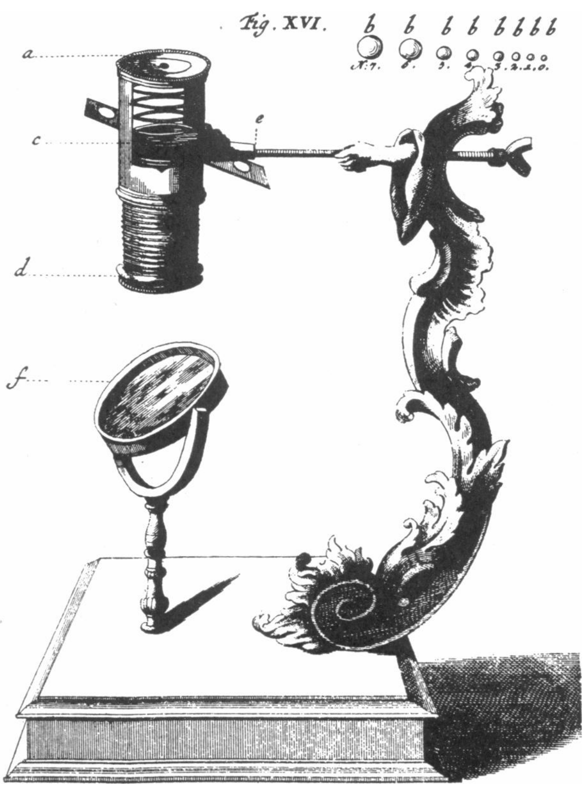

Fig. 4.—Ledermuller's "simple" microscope. (a) The lens holder, (b) the different lenses used, (c) glass object carrier, (d) location of mirror, (e) screw carrier for microscope tube, (f) concave mirror.

From anatomical evidence derived from dissection Réaumur apparently believed that bees were fertilized by copulation, but it may be recalled that he described a "spiral matrix" in a viviparous fly, which he said was composed of two thousand maggots arranged lengthwise. This is amazing from one who knew insects so well, although perhaps no more so than many other statements made in the early or the present history of science. It seems that Réaumur also investigated the occurrence of malformations, and one of his most ingenious experiments on reproduction will be spoken of in connection with Spallanzani.

SWAMMERDAM

Swammerdam, who delighted and excelled in dissections, experimented on the effect of mechanical injury upon developing pupae of the butterfly and found that he could produce malformations. He also experimented with mating snails and frogs and carefully described the occurrence of internal fertilization in the former and that of external in the latter. His description of the behavior of snails at the time of mating is very engaging and probably could not be improved much by contemporary behaviorists. While feeding young tadpoles, the development of which he was observing, on ova removed from the body of an unmated female frog, he noticed that those that were not eaten by the tadpoles failed to develop while the fertilized ones always did so. He also placed fertilized frog ova in various liquors, one day after laying, for the purpose of coagulating the albumen in order to make the removal of the albumen easier, and enable him to observe the embryos better, but he concluded that he always damaged them, although we now know that frog eggs do not contain embryos at that time. Swammerdam, like his successor Spallanzani, mistook the pigment spot in the frog egg for the young tadpole, for he too was a preformationist and ovist. It is regrettable that he did not state what the liquors were in which he placed the eggs and whether he also attempted to remove the albumen somewhat later in development. It would seem that he must have tried to do so. Being a preformationist, Swammerdam, like Haller and others, held that malformations also are preformed in the germ. Morgani, who was impressed with the changes produced by disease, thought that it was the cause of abnormal development and others looked to accident. However, the theory of epigenesis opened a door of hope and gave impetus to the study of the origin of monsters.

In spite of his many thorough investigations on and dissections of insects, Swammerdam concluded that the frog should be classed with them, and it may be recalled that Réaumur placed alligators and crocodiles among arthropods. Swammerdam believed that man and the frog pass through the same developmental stages as insects; that is, of an egg, a worm, a nymph (pupa) before reaching maturity. He also observed bees and experimented with them but, contrary to Réaumur, concluded that the female is impregnated by an aura. Since Swammerdam had found that frog ova are fertilized externally his return to an old error is all the more surprising.

CROSS-FERTILIZATION

Up to about the middle of the nineteenth century the attention of embryologists was focused mainly upon reproduction, the genesis of form, the relationships of organs and upon comparative embryology and phylogeny. The accumulation of many facts regarding the structure and form of the embryo was necessary before it was possible to undertake experimentation, but one need only recall that the keeping of bees dates far back in human history in order to realize that many experiments undoubtedly were made in this connection. The same thing probably holds for hybridization, for the "mule" among plants and animals very naturally excited great curiosity and speculation and it is likely that the breed of hybrids we still call mules has been produced from time immemorial. The fact that they were sterile could not fail to arouse curiosity and must have stimulated attempts to produce similar forms in other species. The crossing of the partridge and the domestic fowl, of dogs and foxes, must be things of the distant past, and for race crossing among men slavery offered abundant opportunity. It must have seemed anomalous that they are fertile.

(To Be Continued)

WILLIAM STEWART TAYLOR
1847-1931

A TRIBUTE TO A CALIFORNIA PHYSICIAN

By MARTIN H. FISCHER, M. D.
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"FOR forty-six years a practitioner of medicine in this valley." These are the significant words that are engraved upon the marker of William Stewart Taylor's grave. The casual reader may see in these words only the sign of a long and arduous service; those of better understanding will find in them a monument to all that medical teachers and medical schools have striven for and all that a suffering humanity of the past or the present has ever cried for.

William Stewart Taylor became a piece of his time at eighteen when, at the close of the Civil War, he floated down the Ohio from Pittsburgh to St. Louis. The army was there disposing of its mules and as the driver of a six-mule plains wagon he joined a caravan of such, bound West. The nights, beginning with the first, were broken by the circular ridings of Indians. "Not to die" was to become a part of that spirit of the West whose marks were silence, long-suffering, endurance, and fortitude.

With some five years of such discipline to his credit he made his way back to the home town of Saltsburg, in Pennsylvania, and after "reading" medicine with the doctor of his village he went to Philadelphia, where, in 1874, he had bestowed upon him the medical degree of Jefferson Medical College. He went almost at once to California and after a season in San Francisco, wishing to work with man where man touches his world most directly, he settled in the village of Livermore in the basin of California's sumptuous Livermore Valley. Her people were ranchers, her wealth was the wealth of fruits and animals, and her intelligence was that which comes from immediate contact with the soil. The wealth that springs from the accident of natural resources never came to the pioneers of the Livermore Valley.

The youthful Taylor came as first physician into this empire. As her population increased others came, but Taylor remained the first.

What kind of mental capital could the most competent of practitioners bring to any community in A. D. 1876? The medical hazards of life were the hazards of epidemic disease and its surgical hazards, those that spring from infection, from pregnancy, and from accident. All medicine came to young Taylor's door; and whatever its nature it had to be met by Taylor, and by him alone. To say, therefore, that he was a man of capacity, that he was skilled in the administration of medicine, skilled as an obstetrician, skilled as a surgeon, is to state the obvious. The practitioner of those days had to be these things or perish.

But the handicaps under which the medical and surgical knowledge of that day had to be applied added difficulties unknown today, for what is now school-boy knowledge was then unborn. The mere existence of microörganisms was still being denied; bacteria as the causes of disease were just being suggested—and flouted; disease as the expression of specific infection was hypothesis and surgery without pus was unimaginable. The turn came a decade after Taylor's graduation and few were the men who, born into the preantiseptic and the preaseptic schools of medical thought, could make the change to the new. Taylor did.

But this first change in his point of view regarding fundamentals in medical theory and medical practice was only the beginning of a series of such that he had to overcome. In surgery mere mechanical deftness had to ally itself with an understanding of the nature of disease, and in obstetrics the red flare of childbed fever had to cease being an act of God to become something more closely related to malpractice. In medicine, dropsy, fever, and peritonitis had to cease being diseases and to appear as the products of more primary disasters; while infection with specific microörganisms had to bring with it the at once simplifying and complicating concepts of specific